REMARKS

Upon entry of the present Amendment, 25-41, 44-48 and 65-78 will be pending. Claims 1-24, 42, 43 and 49-64 are withdrawn from consideration and/or canceled. Applicants reserve the rights to pursue the withdrawn and/or canceled subject matter in a subsequent application.

Rejections under 35 U.S.C. § 112

Indefiniteness

Claims 25 and 44 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

The Examiner made the following specific rejections:

The current amendment to the claims adds the limitation "non-movably" to the piezoelectric transducer and electrode elements but Applicants fail to show specific support for this limitation in the text of the specification and contrary to Applicants suggestion, drawings do not aid in illustrating this limitation. Only electrodes are shown in the figures and it is known in the art that electrodes in microfluidic devices are stationary. Examiner requests removal of this limitation as it is redundant.

Applicants respectfully disagree and submit that the specification and the drawings as originally filed provide ample support for the limitation "non-movably." For example, at page 38, lines 10-15, the speciation, referring to Figure 5, describes that "the whole bottom wall 220 is a piezoelectric transducer" and the piezoelectric transducer is used to produce an acoustic wave. The piezoelectric transducer may be bound to a solid plate from the top or bottom side. *See e.g.*, page 39, lines 2-7 of the present specification. The piezoelectric transducer is non-movably adapted along a portion of the chamber, *i.e.*, not moved relative to the chamber during use. Similarly, at page 39, lines 16-24, the speciation, also referring to Figure 5 (including Figures 5A and 5B),

describes electrode elements employed for generating an electric field. The metal films or other electrically conductive material can be coated on the surface of the top or bottom plate. *See e.g.*, page 39, lines 18-20 of the present specification. The electrode elements are non-movably adapted along a portion of the chamber, *i.e.*, not moved relative to the chamber during use. Applicants also disagree with the Examiner's statement that the limitation "non-movably" is redundant because, as discussed below in detail, this limitation is one of the features that distinguishes the presently claimed apparatuses from Yasuda, which teaches the use of ultrasonic wave oscillators 31 and the acoustic lens 32 that are movable during use (*See* Yasuda at column 10, lines 26-27).

It is respectfully submitted that the rejection of claims 25 and 44 under 35 U.S.C. § 112 is overcome by the above remarks and/or amendments and must be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 25-41, 44-48, 65-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yasuda, *et al.* (US 6216538) in view of Becker, *et al.* (US 6294063).

This rejection is respectfully traversed. First, Applicants disagree with the Examiner's assertion that Yasuda teach an electrophoretic and acoustic force apparatus for field flow fractionation with carrier medium. Most of the teachings of Yasuda cited by the Examiner are directed to the use of electrophoretic force or acoustic force alone, not in combination. *See e.g.*, Yasuda at: col. 3, line 19-35 (acoustic force alone); col. 7, line 15-20 (compressible v. incompressible fluid); col. 9, line 58-63 (acoustic force alone); col. 12, line 63 (acoustic force alone). The only teachings about the use of electrophoretic force and acoustic force in combination in Yasuda are for cell fusion (Figures 10 and 11, col. 10, line 19 through col. 11, line 24) and gel-electrophoresis (Figures 13, col. 15, line 36 through col. 16, line 28).

The use of electrophoretic force and acoustic force in combination for cell fusion and gel-electrophoresis, as taught in Yasuda, is very different from the use of electrophoretic force and acoustic force in field flow fractionation, as presently claimed. One of the limitations of the presently claimed apparatuses and methods is "a chamber having at least one inlet port and at least

one outlet port, said chamber having such structural characteristics that when a carried medium is caused to travel through said chamber, the traveling velocity of said carried medium at various positions within said chamber is different" (*See e.g.*, Section a) of claims 25 and 44). Regardless whether Yasuda teaches an inlet or an outlet, cell fusion must be conducted in a closed system and there can be no traveling fluid, as shown in Figures 10-12 of Yasuda. Without a traveling fluid, there would be no traveling velocity of the carried medium, let alone different traveling velocities of the carried medium at various positions within a chamber. In gel-electrophoresis, traveling velocity of a carried medium at various positions is the same, not different.

In addition, none of the apparatuses taught in Yasuda uses both at least two electrode elements to cause at least one electrophoretic force having components normal to the traveling direction of the carrier medium on a matter in the carrier medium and at least one piezoelectric transducer to cause at least one acoustic force having components normal to the traveling direction of the carrier medium on a matter in the carrier medium. For example, in the apparatuses shown in Figure 10 of Yasuda, the electrodes 33 are used to cause cell fusion and are not used to maintain cell positions (*See* Yasuda at column 10, lines 19-45). Only acoustic force is used to maintain or change cell positions. *Id.* Similarly, the apparatuses shown in Figure 11 of Yasuda does not use both electrophoretic force and acoustic force. At column 11, lines 18-24, Yasuda teaches:

> In this embodiment, ultrasonic waves are used as the means for trapping a particle as a target, and means for causing a chemical substance to act locally is used as the cell fusion means. However, the means for supplying the chemical substance for local action with this micro-pipetting unit may be used when a cell is trapped by pipette suction, an electric field trap, an optical trap, etc (emphasis added).

This teaching shows that the cell is trapped by either acoustic force or electrophoretic force, but not both. At column 12, lines 1-3, Yasuda teaches:

> Instead of using ultrasonic waves, other methods such as applying an electric field or adding a cell fusion accelerator may be used.

This teaching shows that, for the apparatuses shown in Figure 12 of Yasuda, electrophoretic force is only used for cell fusion, not for positioning the cell. For the apparatuses shown in Figure 13 of Yasuda, electrophoretic force is used to drive particle movement in the gel-electrophoresis (*See*

Yasuda at column 15, line 36 through column 16, line 27). Accordingly, the electrophoretic force is in the direction of particle movement, not normal to the direction of the particle movement.

Further, the presently claimed apparatuses require that at least two electrode elements be non-movably adapted along a portion of the chamber and the at least one piezoelectric transducer be non-movably adapted along a portion of the chamber. Both electrode elements and the piezoelectric transducer are used to generate electrical force and acoustic force having components normal to the traveling direction of the carrier medium. The teaching of Yasuda is in complete contrast in this aspect. For example, the apparatuses shown in Figure 10 of Yasuda are used to promote cell fusion. The ultrasonic wave oscillators 31 and the acoustic lens 32 are used to trap a cell at the focal point of ultrasonic waves (*See* Yasuda at column 10, lines 26-27). In order to do that, the position of the focal point can be moved by moving a unit, including the ultrasonic wave oscillator 31 and the acoustic lens 32 by a three-dimensional manipulation unit 35. Making the ultrasonic wave oscillators 31 and the acoustic lens 32 non-movably adapted along a portion of the chamber, as required by the present claims, would render the apparatuses shown in Figure 10 of Yasuda inoperable. For the same reason, the pair of two-dimensional arrays of transducers 39, as shown in Figure 12 of Yasuda, cannot be non-movably adapted along a portion of the chamber. The apparatuses shown in Figure 13 of Yasuda are used in gel-electrophoresis. Accordingly, the electrophoretic force must be in the direction of particle movement, but cannot be normal to the direction of the particle movement.

The Examiner also relied on inherent disclosure of Yasuda, *e.g.*, "a tube inherently has an inlet and outlet" and "inherently has an array of electrodes." Applicants respectfully submit that this analysis is incorrect. While there is a doctrine for "inherent anticipation," there is no such inherency doctrine for obviousness analysis.

Becker does not cure the defects of Yasuda for a number of reasons. First and foremost, the Examiner's analysis is flawed because the Examiner combined the teachings of two unrelated Becker patents, *i.e.*, Becker, *et al.* (US 6294063) ('063 patent) and Becker, *et al.* (US 5888370) ('370 patent) as teachings of a single reference without any explanation why this should be the case. The following details the Examiner's citation of the two Becker patents:

- multiple inlet and outlet ports in an electrophoretic field flow fractionation apparatus as well as an array of electrodes (col. 4, I. 46 - col. 5, I. 3) for manipulation of sample (Figures 9, 9B, 11, 12, 13) - **the '063 patent**;

- a chamber with at least one inlet port and at least one outlet port (col. 3, I. 26-28) with at least two electrode elements and preferably an electrode array disposed along a portion of the chamber energized by an electrical signal generator to create an electrical field to cause an electrophoretic force normal to the traveling direction of a carrier medium, (col. 3, I. 49 - col. 4, I. 10, 35-40) whereby the chamber may be a tube (col. 28, I. 1-2) - **the '370 patent**;

- the AC or DC signal generator can be connected to a plurality of electrical conductor buses connected to more than two individual electrode elements (col. 7, I. 16-36; col. 20, I. 34-56) - **the '370 patent**;

- alternately, electrode elements can be adapted longitudinally or latitudinally along the inside or outside of the chamber whereby the array may be parallel, interdigitated, castellated, polynomial or plane (col. 4, I. 1-40, 47-50) - **the '370 patent**;

- electrode elements are made of metallayer(s) on the surface of the chamber, particularly gold and chromium (col. 7, I. 16-21; col. 20, I. 56-62) - **the '370 patent**;

- these elements create a spatially inhomogeneous electric field (col. 5, I. 9-20) to vary the magnitude and frequency of the electrical signals (col. 4, I. 64 - col. 5, I. 8) - **the '370 patent**;

- Becker teaches .introducing a medium into the apparatus (Example I, col. 16, I. 16 - col. 17, I. 51) and into the chamber giving a velocity profile and applying at least one electrical signal to provide an electrophoretic force on the medium

normal to the traveling direction of the carrier medium and a second electrical signal used to generate an acoustic wave to displace matter normal to the direction of the carrier medium - **the '370 patent**; and

- Since the programmable manipulation force can be a dielectrophoretic force, electrophoretic force, an optical force or a mechanical force (ultrasonic force - col. 7, I. 63 - col. 8, I. 5) therefore it also inherently has the ability to move a packet by electrophoretic or ultrasonic movement depending on whether the force generator is DC or AC and the frequency of the AC as modulated by the controller for the force generator - **the '063 patent**.

There is no explanation as to why the skilled artisans would be motivated to combine the two unrelated Becker patents with each other or to combine Yasuda with the Becker patents. Indeed the skilled artisans would not be motivated to combine the cited references. The '370 patent, while teaching field flow fractionation devices and methods, uses electrophoretic force only and does not teach the use of both electrophoretic force and acoustic force in field flow fractionation. The '063 patent, which teaches methods and apparatuses for microfluidic processing by programmably manipulating a packet, has nothing to do with field flow fractionation at all.

It is respectfully submitted that the rejections of claims 25-41, 44-48, 65-78 under 35 U.S.C. § 103 have been overcome by the above remarks and/or amendments and must be withdrawn. Early allowance of the pending claims 25-41, 44-48 and 65-78 are earnestly requested.

Finality

The Examiner stated that applicant's amendment necessitated the new ground(s) of rejection to support the finality of the rejections. However, there is no explanation how Applicant's amendments necessitated the final rejections. In addition, the Examiner combined the teachings of two unrelated Becker patents as teachings of a single reference without any explanation why this is permissible. Indeed, the '370 patent was used in combination with Cannon and/or Yasuda in the October 22, 2002 Office Action (Paper No. 9) and the rejection based on the '370 patent was later

withdrawn in the April 8, 2003 Office Action (Paper No. 12). Accordingly, the applicants respectfully request that the finality of the present rejection be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant(s) petition(s) for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or fees due in connection with this document to **Deposit Account No. 03-1952** referencing docket no.471842000200. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: December 2, 2003

Respectfully submitted,

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